UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

GILDA HAGAN-BROWN, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Case No. 1:14-cv-01614-AJT-JFA Hon. Anthony J. Trenga Hon. John F. Anderson
JANINE ALI, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Case No. 1:14cv-01615-AJT-JFA Hon. Anthony J. Trenga Hon. John F. Anderson

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANT'S MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

It is well understood that patients who discontinue antidepressant treatment may experience symptoms (including, for example, dizziness or nausea) upon stopping therapy. Since Defendant Eli Lilly and Company ("Lilly") brought Cymbalta to market in 2004, the labeling for the medicine has provided a detailed, three-paragraph warning about this risk, identifying the most common symptoms and informing doctors that they occurred at a rate significantly higher than seen with placebo-controlled patients.

Plaintiffs Janine Ali and Gilda Hagan-Brown, who took Cymbalta in 2012 and 2013, respectively, have filed complaints with a myriad of claims regarding the Cymbalta label. Of their claims, the only recognizable ones are Plaintiffs' negligent failure to warn claims, which allege that Lilly's warnings -- which described the very discontinuation symptoms they allegedly experienced -- were insufficient to advise their respective physicians of this potential risk. These claims fail as a matter of law because Cymbalta's warning is legally adequate under well-established Virginia law. Ms. Ali's negligent failure to warn claim fails for the additional reason that different warnings would not have affected her doctor's prescribing decision.

LISTING OF UNDISPUTED FACTS

A. Cymbalta

Lilly manufactures Cymbalta (duloxetine hydrochloride), a serotonin and norepinephrine reuptake inhibitor ("SNRI"). *See* Cymbalta U.S. Physician Package Insert § 11 (Sept. 2011), Declaration of Emily Ullman ("Ullman Decl.") (June 29, 2014), Ex. 1. Since first applying to the FDA in 1991 to study Cymbalta, Lilly has conducted dozens of studies on the medicine. *See* Letter to FDA from Lilly, CYM-00526490 (June 3, 1991), Ullman Decl. Ex. 2; Cymbalta (LY248686), Clinical Study Results 1-3, *available at* http://lillytrials.com/results/Cymbalta.pdf, Ullman Decl. Ex. 3. These studies have shown Cymbalta to be effective in treating a wide range of conditions, resulting in FDA approvals of Cymbalta for the treatment of major depressive disorder (2004), fibromyalgia (2008), and chronic musculoskeletal pain (2010), among other conditions. Letter to Lilly from FDA, CYM-00727991 (Aug. 3, 2004), Ullman Decl. Ex. 4; Letter to Lilly from FDA, CYM-01183976 (June 13, 2008), Ullman Decl. Ex. 5; Letter to Lilly from FDA, CYM-00304561 (Nov. 4, 2010), Ullman Decl. Ex. 6.

It has long been understood in the medical community that patients stopping any antidepressants may experience so-called discontinuation-emergent adverse events ("DEAEs"),

or discontinuation symptoms, and should be clinically managed accordingly. *See, e.g.*, Am. Psych. Ass'n, Practice Guideline for the Treatment of Patients with Major Depressive Disorder 20 (3d ed. 2010), *available at* http://psychiatryonline.org/pdfaccess.ashx?ResourceID=243261&PDFSource=6 ("To minimize the likelihood of discontinuation symptoms, patients should be advised not to stop medications abruptly and to take medications with them when they travel or are away from home. A slow taper or temporary change to a longer half-life antidepressant may reduce the risk of discontinuation syndrome when discontinuing antidepressants or reducing antidepressant doses."), Ullman Decl. Ex. 7.

Lilly collected and analyzed data about DEAEs as part of many of its Cymbalta clinical trials. *See, e.g.*, Clinical Synopsis: Study F1J-MC-HMAQ Study Group A (Nov. 16, 2004), Clinical Study Results at 116, *available at* http://lillytrials.com/results/Cymbalta.pdf, Ullman Decl. Ex 3. That data was summarized and submitted to the FDA, both before Cymbalta's approval and then on an ongoing basis as additional data became available. *See, e.g.*, Complete Response to FDA Approvable Letter NDA 21-427, App. 9.2.9 (Mar. 24, 2003), CYM-00708136-8143 (providing consolidated DEAE data from six pre-approval clinical trials), Ullman Decl. Ex. 8; Reports of Analyses of Data from More than One Study for Cymbalta (Duloxetine hydrochloride) Chronic Pain tbls. 3.36 & 3.37 (May 12, 2009), CYM-00195110-5168 (providing consolidated DEAE data from a 48-study data set), Ullman Decl. Ex. 9.

Lilly also published detailed DEAE information from its pre-approval studies. *See, e.g.*, Christer Allgulander et al., *Pharmacotherapy of Generalized Anxiety Disorder: Results of Duloxetine Treatment from a Pooled Analysis of Three Clinical Trials*, 23 Current Med. Research & Opinion 1245 (2007), Ullman Decl. Ex. 10; David G. Perahia et al., *Symptoms Following Abrupt Discontinuation of Duloxetine Treatment in Patients with Major Depressive*

Disorder, 89 J. of Affective Disorders 207 (2005), Ullman Decl. Ex. 11. Lilly's publications included a 2005 article by three Lilly employees and an academic researcher (the "Perahia article") that reported the very rates of DEAEs that Plaintiffs have accused Lilly of concealing. *See* Perahia et al., *supra*; Compl., *Ali*, Dkt. 1, ¶¶ 21-22 (Nov. 26, 2014).

Based on Lilly's sharing of its clinical trial data with the FDA, the initial Cymbalta label carried detailed warnings related to discontinuation symptoms in both the *Precautions* and *Dosage and Administration* section. Letter to Lilly from FDA at CYM-00728000-02, CYM-00728012 (Aug. 3, 2004), Ullman Decl. Ex. 4.

By April 2012, before either Plaintiff used Cymbalta, Lilly had updated its discontinuation warnings numerous times to account for new clinical data, ongoing clinical experience, and revised guidance from FDA. *See* Expert Report of Karen M. Becker, PhD ("Becker Report"), *Ali* / *Hagan-Brown*, at 15-16 (May 14, 2015), Ullman Decl. Ex. 12. By 2012, the "Highlights" section on the very first page of the Cymbalta label prominently warned about the risk of discontinuation under the bolded "**WARNINGS AND PRECAUTIONS**" heading:

- Discontinuation: May result in symptoms, including dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis. (5.7).

2011 Label at 1, Ullman Decl. Ex. 1. The Highlights section also warned about the need to taper: "Discontinuing Cymbalta: A gradual dose reduction is recommended to avoid discontinuation symptoms. (5.7)." *Id.*

The label then provides more detailed information on this risk in sections that were cross-referenced in the first-page Highlights section:

DOSAGE AND ADMINISTRATION

2.4 Discontinuing Cymbalta

> Symptoms associated with discontinuation of Cymbalta and other SSRIs and SNRIs have been reported. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible *[see Warnings and Precautions (5.7)]*.

Id. § 2.4.

> **WARNINGS AND PRECAUTIONS**
>
> **5.7 Discontinuation of Treatment with Cymbalta**
>
> Discontinuation symptoms have been systematically evaluated in patients taking duloxetine. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at 1% or greater and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis.
>
> During marketing of other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. Although these events are generally self-limiting, some have been reported to be severe.
>
> Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate *[see Dosage and Administration (2.4)]*.

Id. § 5.7.[1]

[1] The second and third paragraphs of this warning were "class labeling" for all SNRIs and SSRIs, written by the FDA. *See* Letter from Russell Katz, M.D., Center for Drug Evaluation & Research, U.S. Food & Drug Admin., to Wyeth Pharmaceuticals Inc., at 4 (Mar. 19, 2004) ("Additionally, we are taking this opportunity, in a class labeling initiative for all of the selective (continued…)

The label underwent additional slight revisions after Ms. Ali began Cymbalta but before Ms. Hagan-Brown did. *See* Cymbalta U.S. Package Insert ("2012 Label") (Sept. 2012), Ullman Decl. Ex. 13. The discontinuation symptoms listed in the Highlights section and section 5.7 were reordered to reflect changes in their relative frequencies in updated clinical trial data. *Compare id*. at 1 *with* 2011 Label at 1, Ullman Decl. Ex. 1; *see also* Deposition of Christine Phillips, PhD., at 189:18-190:22 (July 18, 2014), Ullman Decl. Ex. 14. A patient counseling section addressing discontinuation was also added:

> **17.11 Discontinuation of Treatment**
>
> Patients should be instructed that discontinuation of Cymbalta may be associated with symptoms such as dizziness, headache, nausea, diarrhea, paresthesia, irritability, vomiting, insomnia, anxiety, hyperhidrosis, and fatigue, and should be advised not to alter their dosing regimen, or stop taking Cymbalta without consulting their physician *[see Warnings and Precautions (5.7)]*.

2012 Label § 17.11, Ullman Decl. Ex. 13.

Lilly also provided warnings to patients about Cymbalta's discontinuation risk through a Medication Guide, a risk communication written for the patient in patient-friendly language and required by federal law to be dispensed at the pharmacy with the medication. *See* 21 C.F.R. § 208.20(a)(1) (2013); 21 C.F.R. § 208.24(e) (2013). Prior to 2012, all antidepressants utilized the same, non-drug specific Medication Guide that FDA had promulgated to focus on the potential risks of suicidal thoughts with all antidepressants. The pre-2012 version of this

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serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs), to change labeling in regards to discontinuation symptoms . . . ."), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/020151_S032_EFFEXOR_TABLETS.pdf, Ullman Decl. Ex. 15. As a result, Celexa, Effexor, Lexapro, Paxil, and Zoloft all bore nearly identical paragraphs around the time of Cymbalta's initial approval, including instructions to taper the dose of the medication upon discontinuation. *See id.* (mandating the second and third paragraphs in the Effexor label); Becker Report at 19-20 (citing FDA-approved labeling), Ullman Decl. Ex. 12.

Medication Guide also noted under the bolded headline "**What else do I need to know about antidepressant medicines?**":

- **Never stop an antidepressant medicine without first talking to a healthcare provider.** Stopping an antidepressant medicine suddenly can cause other symptoms.

Medication Guide at 2 (Dec. 4, 2008), Ullman Decl. Ex. 16.

In August 2012, approximately one month before Ms. Hagan-Brown was first prescribed Cymbalta, Lilly issued a new, Cymbalta-specific Medication Guide that elaborated further on the risk of discontinuation symptoms:

> **Do not stop Cymbalta without first talking to your healthcare provider.** Stopping Cymbalta too quickly or changing from another antidepressant too quickly may result in serious symptoms including:
>
> - anxiety, irritability
> - feeling tired or problems sleeping
> - headache, sweating, dizziness
> - electric shock-like sensations
> - vomiting, nausea, diarrhea

Medication Guide ("2012 Medication Guide") (Aug. 2012), Ullman Decl. Ex. 17.

B. Plaintiff Janine Ali

Plaintiff Janine Ali is a 63-year-old woman who has long suffered from chronic pain. Deposition of Janine Ali ("Ali Dep.") at 8:7-11 (Apr. 8, 2015), Ullman Decl. Ex. 18; Deposition of Navera R. Ahmed, M.D. ("Ahmed Dep.") at 35:14-36:5 (Apr. 20, 2015), Ullman Decl. Ex. 19. In the fall of 2006, Ms. Ali began seeing rheumatologist Dr. Navera Ahmed for complaints of frequent and severe back pain, as well as other pain issues, along with insomnia and fatigue. *See* ALIJ-AHMEDN-0074, 82-83, 85, 86, Ullman Decl. Ex. 20; ALIJ-ACNV-0014-15, Ullman Decl. Ex. 21. After an examination revealing that Ms. Ali had muscle pain, joint pain, and showed all

of the eighteen "tender points" that are indicative of fibromyalgia, *see* Expert Report of Dr. Michael Clark at 3 (May 14, 2015), Ullman Decl. Ex. 22, Dr. Ahmed diagnosed her with that condition and osteoarthritis. *See* ALIJ-AHMEDN-0074, 82-83, 85, 86, Ullman Decl. Ex. 20; ALIJ-ACNV-0014-15, Ullman Decl. Ex. 21.

Still experiencing tender points, osteoarthritis, and pain in October 2009, Ms. Ali expressed interest in switching treatment from physical therapy and muscle relaxants. Ahmed Dep. at 41:22-42:22, Ullman Decl. Ex. 19. Dr. Ahmed provided her with Cymbalta's package insert and discussed the risks and benefits of the medication. *Id.* at 42:21-43:22. Dr. Ahmed believes it was "more likely than not" that she would have reviewed discontinuation risk with Ms. Ali at that time. *See id.* at 44:1-14, 46:6-16. After additional consideration, Ms. Ali stated on her next visit to Dr. Ahmed, approximately one week later, that she did not want to try Cymbalta. *See* ALIJ-AHMEDN-0026, Ullman Decl. Ex. 20.

However, in April 2012, unable to control her musculoskeletal pain and suffering from "poor energy," Ms. Ali reconsidered Cymbalta based on Dr. Ahmed's recommendation. Ahmed Dep. at 54:22-56:17, Ullman Decl. Ex. 19. Dr. Ahmed prescribed her 30 milligrams of Cymbalta per day in May 2012. *Id.* at 58:11-19. At that time they again discussed the benefits and risks of Cymbalta. *See id.* at 58:19-20.

Ms. Ali reported to Dr. Ahmed in June 2012 that Cymbalta was "helping a lot" with her pain. ALIJ-AHMEDN-0008, Ullman Decl. Ex. 20. Seeing this positive response, Dr. Ahmed increased her dose to the recommended 60 milligrams per day. Ahmed Dep. at 60:19-61:3, Ullman Decl. Ex. 19. Nonetheless, in early July, Ms. Ali unilaterally and without the benefit of Dr. Ahmed's medical advice decided to stop taking Cymbalta. *See id.* at 74:4-6; Ali Dep. at 159:2-160:3, 169:19-170:11, Ullman Decl. Ex. 18. While the precise contours of her taper

period remain unclear, Ms. Ali states that during her tapering period she experienced "angriness, sad[ness], having nightmares," Ali Dep. at 171:17-20, Ullman Decl. Ex. 18, "sweats, . . . crying periods, . . . depression, . . . craziness," *id.* at 173:20-174:2, and changes in her emotions towards her husband. *Id.* at 172:6-11. She did not seek treatment for any of these symptoms, however, or discuss them with a doctor other than as a friend between July and November. *Id.* at 175:15-176:7.

By the time Ms. Ali visited Dr. Ahmed again in November 2012, she had already seen a website discussing other individuals who allegedly suffered from Cymbalta discontinuation and had been in contact with an individual who "may have been an attorney or paralegal about Cymbalta." *See* Ali Dep. at 23:17-24:3, 31:16-33:7, Ullman Decl. Ex. 18; Pl.'s Resps. to Def.'s Second Set of Interrogatories at 2 (May 29, 2015), Ullman Decl. Ex. 23. She was also "over . . . the worst of [her symptoms]" and was "much better." Ali Dep. at 170:20-171:6, 174:14, Ullman Decl. Ex. 18. By February 2013 they were "all gone." *Id.* at 173:20-174:4.. None of the prior, unreported symptoms Ms. Ali now alleges prevent her from carrying out her life activities today. *See id.* at 57-59.

C. Plaintiff Gilda Hagan-Brown

Plaintiff Gilda Hagan-Brown is a 52-year-old woman who has had a striking history of personal tragedy: her adult son went missing in 2001 and was never found, Deposition of Gilda Hagan-Brown ("Hagan-Brown Dep.") at 73:18-74:15 (Apr. 7, 2015), Ullman Decl. Ex. 24; she took time off work to care for her sisters, one of whom had breast cancer and the second of whom underwent prophylactic removals of her breasts and ovaries, *id.* at 26:12-17, 29:8-30:5, 30:8-31:7; she had ovarian surgery and accompanying premature menopause in November 2011, *id.* at 33:14-34:1, 36:9-19; her daughter had to be pulled out of a prestigious school to which she had been given a scholarship due to racial bullying, *id.* at 256:12-22; she quit work in February

2012 due to severe pain that was making it difficult for her to focus at work, and suffered severe financial strain as a result, *id.* at 255:5-15; and she unsuccessfully sought disability coverage to alleviate that strain, *id.* at 261:12-263:22. Unsurprisingly, these various tragedies were accompanied by the very symptoms she attributes to Cymbalta: worry, sadness, depression, anxiety, moodiness, sweating, dizziness, dry mouth, and migraines. *Id.* at 78:15-79:12.

In September 2012, Ms. Hagan-Brown suffered another setback when she was diagnosed with fibromyalgia (and "some elements of depression") after seeking treatment for pain throughout her body, migraines, weight gain, and insomnia. Deposition of Mohammad Bahadori, M.D. ("Bahadori Dep.") at 24:6-25, 25:3-17, 35:11-18 (Apr. 17, 2015), Ullman Decl. Ex. 25; BrownG-BahadoriM-0002, 0010, Ullman Decl. Ex. 26; BrownG-ACC-0008-11, Ullman Decl. Ex. 27. Her doctor, Dr. Mohammad Bahadori, prescribed Ms. Hagan-Brown 30 milligrams per day of Cymbalta. *See* BrownG-Pltf-0040, Ullman Decl. Ex. 28.

Ms. Hagan-Brown elected to discontinue Cymbalta in February 2013 after continuing to experience pain and after experiencing "brain fuzziness" from a combination of Cymbalta and Wellbutrin. *See* BrownG-BahadoriM-0008,0010, Ullman Decl. Ex. 26, BrownG-ACC-0013, 0062, Ullman Decl. Ex. 27 , BrownG-Pltf-0056, Ullman Decl. Ex. 28. Dr. Bahadori's medical records also state that she told him that Cymbalta was too expensive. Bahadori Dep. at 57:11-17, Ullman Decl. Ex. 25. It is unclear whether Ms. Hagan-Brown undertook her discontinuation under Dr. Bahadori's supervision, but she recalls tapering between February 20, 2013 and March 9, 2013 using a two-week supply of 30 milligram Cymbalta samples. *See* Hagan Brown Dep. at 153-157, Ullman Decl. Ex. 24. She believes that she took one pill every other day for a week but does not recall the remainder of her tapering regimen. *Id.* at 156:19-157:1.

Dr. Bahadori's notes from Ms. Hagan-Brown's first appointment with him after her discontinuation reflect only that Ms. Hagan-Brown was "fuzzy in her head and discontinued Cymbalta." Bahadori Dep. at 52:5-9, Ullman Decl. Ex. 25. Ms. Hagan-Brown has claimed a broader range of symptoms, which largely track the symptoms she reported pre-Cymbalta, from her other major life stressors:

> 1) moodyness [sic] /depression/anxiety (frustration/tears); 2) dizzyness [sic] /buzzing feeling in head and eyes/electric shock feeling in head 3) nausea/diarrhea; 4) dry eye/blurry vision/glazed over eyes/irritated; 5) dry mouth; 6) migraines ; 7) hair loss; 8) insomnia; 9) night sweats/day sweats; 10) sensitive to light; 11) weight gain; 12) pain and stiffness; 13) forgetfullness [sic]. Loose [sic] train of thought.

BrownG-Pltf-0035, 0038-39, Ullman Decl. Ex. 28. Although Ms. Hagan-Brown applied for disability during the time period her alleged discontinuation symptoms were occurring, she did not mention them on her disability application. *See* Hagan-Brown Dep. at 262:14-263:22, Ullman Decl. Ex. 24.

Ms. Hagan-Brown testified that her claimed discontinuation symptoms began declining between August and October of 2013, with only the "buzzing feeling" lasting until May 2014. *See id.* at 163:22-164:8.

D. Procedural History

On November 26, 2014, Ms. Ali and Ms. Hagan-Brown filed separate suits against Lilly, raising identical causes of action: "negligence," with allegations clarifying that the claim was negligent failure to warn; "design defect"; "failure to warn"; "constructive fraud"; "actual fraud"; and "breach of implied warranty." Compl., *Ali*, at 10-24; Compl., *Hagan-Brown*, Dkt. 1, at 10-24 (Nov. 26, 2014). On May 1, 2015, the Court granted Lilly's motion for judgment on the pleadings and dismissed both Plaintiffs' design defect claims. *See* Order, *Ali*, Dkt. 83 (May 1, 2015).

Cases involving virtually identical allegations have progressed across the country. In December 2013, Lilly obtained summary judgment on the basis of proximate cause in *Carnes v. Eli Lilly & Co.*, No. 0:13-591-CMC, 2013 WL 6622915, at *7 (D.S.C. Dec. 16, 2013). Lilly also obtained summary judgment -- this time on both proximate cause and the adequacy of its warning -- in *McDowell v. Eli Lilly & Co.*, 58 F. Supp. 3d 391 (S.D.N.Y. 2014). Finally, the court denied summary judgment in *Herrera v. Eli Lilly & Co.*, No. CV 13-2702 (C.D. Cal.) and *Hexum v. Eli Lilly & Co.*, No. CV 13-02701 (C.D. Cal.), cases pending in the Central District of California, on the basis of proximate cause. Both the *Herrera* and *Hexum* decisions explicitly declined to reach the issue of adequacy and based the proximate cause rulings on specific plaintiff and prescriber testimony.

ARGUMENT

Summary judgment is appropriate when "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). "Conclusory or speculative allegations do not suffice" to create a genuine issue of material fact, "nor does a 'mere scintilla of evidence'" in support of the non-movant's case. *Thompson v. Potomac Elec. Power Co.*, 312 F.3d 645, 649 (4th Cir. 2002) (quoting *Phillips v. CSX Transp., Inc.*, 190 F.3d 285, 287 (4th Cir. 1999) (per curiam)).

I. LILLY IS ENTITLED TO JUDGMENT AS A MATTER OF LAW ON PLAINTIFFS' "NEGLIGENCE" CLAIM

A. The Cymbalta Warning is Adequate as a Matter of Law.

Plaintiffs' core claims -- for negligent failure to warn -- fail. Under Virginia law, a drug manufacturer has a duty to warn the prescribing physician -- not the patient -- of the risks of a prescription medicine. *Pfizer, Inc. v. Jones*, 272 S.E.2d 43, 44-45 (Va. 1980); *Talley v. Danek Med., Inc.*, 179 F.3d 154, 163 (4th Cir. 1999). The adequacy of a warning may be determined as

a matter of law. *See Pfizer v. Jones*, 272 S.E.2d 43 (finding pharmaceutical warning adequate as a matter of law and granting judgment for defendant); *Kling v. Key Pharms., Inc.*, No. 93-1827, 1994 WL 477815 (4th Cir. Sept. 6, 1994) (granting judgment as a matter of law based on adequate warning). The standard is an objective one and does not rely on the individual testimony of any particular physician. *See, e.g., Pfizer v. Jones*, 272 S.E.2d at 44-45 (finding warning adequate in the face of physician testimony that warning was inadequate); *Kling*, 1994 WL 477815, at *3 (evaluating label adequacy based on language of the warning and not on prescriber's testimony); *cf. Abbot by Abbot v. Am. Cyanamid Co.*, 844 F.2d 1108, 1115 (4th Cir. 1988) ("Virginia law does not support the notion that the treating physician's subjective view as to adequacy conclusively determines that issue.").

Virginia "[c]ourts have routinely held warnings adequate as a matter of law when they alert a party to the very injury for which the plaintiff seeks relief." *Ball v. Takeda Pharm. Am., Inc.*, 963 F. Supp. 2d 497, 504 (E.D. Va. 2013), *aff'd*, 587 F. App'x 78 (4th Cir. 2014).; *see also Pfizer v. Jones*, 272 S.E.2d at 44-45 (holding warning adequate as a matter of law where prescribing physician was "warned of the danger," but "was not told exactly how the danger would operate"); *Kling v. Key Pharm., Inc.*, 1994 WL 477815, at *3 (holding the warning adequate as a matter of law where "[t]he precise harm alleged" by the plaintiff "was clearly listed as a potential side effect"); *Barnette v. E.R. Squibb & Sons, Inc.*, 670 F. Supp. 650, 651-52 (E.D. Va. 1987) (granting summary judgment where the label warned that the harm plaintiff suffered was a possible side effect).

Because a manufacturer's duty to warn runs to the prescribing medical professional, the label must also be assessed in the context of a reader who is "assumed" to "have a certain modicum of basic medical knowledge." *Rule v. Best Indus., Inc.*, No. 96-1624, 1997 WL

499937, at *2 (4th Cir. Aug. 25, 1997); *Talley*, 179 F.3d at 163 ("[T]he information regarding risks is often too technical for a patient to make a reasonable choice." (quoting *Hill v. Searle Lab.*, 884 F.2d 1064, 1070 (9th Cir. 1989)). Moreover, a drug manufacturer need only "give a reasonable warning, not the best possible one." *Ball*, 963 F. Supp. 2d at 504 (quoting *Pfizer v. Jones*, 272 S.E.2d at 45); *Abbot by Abbot v. Am. Cyanamid Co.*, 844 F.2d 1108, 1115 (4th Cir. 1988) ("This issue is whether the warning was reasonable."). Adequacy does not require perfection. *See McDowell*, 58 F. Supp. 3d at 403 ("The warning should also be evaluated as a whole and not through the nitpicking prism of an interested legal advocate after the fact."). The warning need not contain all possible information about a product, such as an explanation of the mechanism of potential harm, *see Pfizer v. Jones*, 272 S.E.2d at 45 (declining to impose on the manufacturer a duty to "explain[]exactly how the danger against which [the plaintiff] had been warned might operate"), or a proscription against every conceivable misuse of the medication, *see Rule*, 1997 WL 499937. Rather, the duty to warn is satisfied by "providing detailed product information" about the instructions for use and the risks associated with the medicine. *Evans v. Mentor Corp.*, No. CIV.A. 1:04-CV-1218, 2005 WL 1667661, at *3 (E.D. Va. June 28, 2005).

It is undisputed that the Cymbalta label informed Plaintiffs' doctors of the "very injur[ies]" for which Plaintiffs are seeking relief. *Ball*, 963 F. Supp. 2d at 504. The *McDowell* court grounded its ruling on this fact, holding the Cymbalta warning adequate pursuant to New York law, which similarly requires that a physician warning "give[] specific detailed information on the risks of the drug." *McDowell*, 58 F. Supp. 3d at 403 (internal quotation marks omitted). As the court noted: "The elements of the Cymbalta discontinuation warning 'portray[ ] with sufficient intensity the risk involved in taking the drug.'" *Id.* at 404 (quoting *Martin v. Hacker*, 628 N.E.2d 1308, 1312 (N.Y. 1993)) (alteration in original). These elements are as follows:

Highlights of Prescribing Information.

The Highlights of Prescribing Information section of the Cymbalta label in effect at the time of Ms. Ali's initial prescription warns that discontinuation "[m]ay result in symptoms, including dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis." 2011 Label at 1, Ullman Decl. Ex. 1. At the time of Ms. Hagan-Brown's initial prescription, the label stated that symptoms included "dizziness, headache, nausea, diarrhea, paresthesia, irritability, vomiting, insomnia, anxiety, hyperhidrosis, and fatigue." 2012 Label at 2, Ullman Decl. Ex. 13.

Dosage and Administration.

The Dosage and Administration section of the Cymbalta label explicitly warns that "[s]ymptoms associated with discontinuation of Cymbalta and other SSRIs and SNRIs have been reported. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible" and directs prescribers to the more detailed warning provided in the label's Warnings and Precautions section. *Id.*

Warnings and Precautions.

The Warnings and Precautions section of the Cymbalta label additionally provides detail on the risks of discontinuation symptoms.

Clear statement of risk. The Cymbalta label plainly sets out the risk of symptoms arising from both "abrupt or tapered discontinuation" and warns that, in placebo-controlled clinical trials, discontinuation symptoms occurred "at a *significantly higher rate* in duloxetine-treated patients compared to those discontinuing from placebo." *Id.* § 5.7 (emphasis added); *see Gurski v. Wyeth-Ayerst Div. of Amer. Home Prods. Corp.*, 986 F. Supp. 654, 654 (D. Mass. 1997)

(granting summary judgment where warning "cautioned the plaintiff specifically regarding the probability, nature, and gravity of the precise condition that she sufficiently suffered").

Detailed identification of possible symptoms. The Cymbalta label includes a detailed catalog of symptoms possible upon discontinuation. Indeed, the very symptoms Plaintiffs allege that they experienced after stopping their Cymbalta treatment are identified in the discontinuation warning. *See Kling*, 1994 WL 477815, at *3 ("The precise harm alleged to be suffered by [Plaintiff] . . . was clearly listed as a potential side effect of taking [the medication]."). Ms. Ali stated at her deposition that upon discontinuation she suffered from "angriness, sad[ness], having nightmares," "sweats, . . . crying periods, . . . depression, . . . craziness," and changes in her emotions towards her husband. Ali Dep. at 171:17-20, 172:6-11, 173:20-174:2, Ullman Decl. Ex. 18. Similarly, the Cymbalta label warned Ms. Ali's doctor that she could experience irritability, dysphoric mood (a medical term for sadness), hyperhydrosis (that is, sweating), agitation, hypomania, and emotional lability. *See* 2011 Label § 5.7, Ullman Decl. Ex. 1. Ms. Hagan-Brown alleges that she suffered, among a large constellation of symptoms, from moodiness; depression; anxiety; dizziness; electric shock feelings in her head; nausea; diarrhea; migraines; insomnia; and sweating. *See* BrownG-Pltf-0035, 0038-0039, Ullman Decl Ex. 28. Each of these symptoms is identified in Cymbalta's label. *See* 2012 Label § 5.7, Ullman Decl. Ex. 13. (The medical term for electric shock sensations is paresthesia. *See id.* ("sensory disturbances (e.g., paresthesias such as electric shock sensations)").)

During the period relevant here, the label listed nearly a dozen discontinuation symptoms that had been observed in Lilly's placebo-controlled clinical trials "at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo" and that occurred above the threshold of "1% or greater": dizziness, nausea, headache, paresthesia, fatigue,

vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis. *Id.* This method of communicating information on individual symptoms appearing in clinical trials is consistent with the accepted practice of identifying such individual adverse events observed at or above a specified threshold and in accord with FDA regulations and guidance directing that the label "list the adverse reactions identified in clinical trials that occurred at or above a specified rate appropriate to the safety database." 21 C.F.R. § 201.57(c)(7); *see also* FDA, *Guidance for Industry: Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products–Content and Format* (Jan. 2006); *McDowell*, 58 F. Supp. 3d at 404. In addition, the label has consistently included an additional subset of potential symptoms reported upon discontinuation of products within the SNRI class, to which Cymbalta belongs, and the selective serotonin reuptake inhibitor ("SSRI") class, and warns that "patients should be monitored" for all of the symptoms identified in the warning. *See* 2011 Label § 5.7, Ullman Decl. Ex. 1.

Given the breadth of the Cymbalta discontinuation warning, Plaintiffs have been left to rest their failure-to-warn claim chiefly on the theory that the warning used a threshold for symptom inclusion ("at 1% or greater . . . and at a significantly higher rate") rather than listing the absolute frequency of each symptom or all of the symptoms combined. *See* Compl., *Ali*, ¶ 21. As *McDowell* recognized, however, courts have "have refused to graft onto the adequacy standard a requirement that a package insert must include specific adverse event frequencies." *McDowell*, 58 F. Supp. 3d at 405 (citing *Hurley v. Lederle Labs., Div. of Am. Cyanamid Co.*, 651 F. Supp. 993, 1002 (E.D. Tex. 1986) and *Percival v. Am. Cyanamid Co.*, 689 F. Supp. 1060, 1064 (W.D. Okla. 1987)).

Potential severity. The discontinuation warning explicitly speaks to the "severity" and "duration" of potential discontinuation symptoms within the SNRI class: "Although these events

are generally self-limiting, some have been reported to be severe." *Id.* More fundamentally, the label specifically identifies symptoms that, by their nature, have the capacity to be severe and that are not, by definition, self-limiting.

Protocol for safe discontinuation. The Cymbalta discontinuation warning devotes a paragraph to advising prescribers of the appropriate means of taking a patient off the medicine. Section 5.1 of Warnings and Precautions advises in connection with warnings about other symptoms: "If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that discontinuation can be associated with certain symptoms." 2011 Label § 5.1, Ullman Decl. Ex. 1. Section 5.7 states: "Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered." *Id.* § 5.7. The recommendation to taper was included in the label based on class-wide guidance from the FDA and on the clinical wisdom of prescribers of antidepressants. *See* Letter from Katz to Wyeth, *supra*, at 4, Ullman Decl. Ex. 5; Deposition of Madeline Wohlreich M.D., *Ali / Hagan-Brown,* at 126:11-13 (Apr. 29, 2015), Ullman Decl. Ex. 29.

Although the adequacy of the label is determined with respect to Plaintiffs' prescribing physicians, the Medication Guides given to Plaintiffs are incorporated into the physician labeling. *See* 2012 Label § 17.2 ("The complete text of the Medication Guide is reprinted at the end of this document."), Ullman Decl. Ex. 13. The Medication Guides reinforce the risk of discontinuation symptoms. The 2012 Guide further emphasizes the potential severity of those symptoms ("may result in serious symptoms") and lists the significant symptoms in patient-

friendly language (e.g. "electric shock-like sensations"). *See* 2012 Medication Guide, Ex. 17. Even Plaintiffs' own regulatory expert, Dr. Louis Morris, agreed that this Guide was adequate to "alert patients of [the] potential concern [of discontinuation] and to talk to physicians if they had issues." Deposition of Louis Morris ("Morris Dep."), *Herrera / Hexum*, at 15:1-12 (Nov. 24, 2014), Ullman Decl. Ex. 30.

Taken together, this comprehensive warning is adequate as a matter of law because it clearly and accurately provides detailed information about the precise harms alleged by Plaintiffs, including their frequency, their severity, and methods for alleviating the associated risk.[2] *See Kling*, 1994 WL 477815, at *3; *Evans*, 2005 WL 1667661, at *3.

B. Ms. Ali Cannot Demonstrate Proximate Cause on her Failure to Warn Claim

Ms. Ali cannot demonstrate that a different warning about discontinuation symptoms would have changed her doctor's decisions to prescribe Cymbalta for her. Under Virginia law, this break in the causal chain between any alleged inadequacy in the Cymbalta discontinuation warning and her injuries is fatal to Ms. Ali's failure-to-warn claim.

A tort plaintiff bears the burden of proving that the defendant was the proximate cause of the injury sustained. *See Sugarland Run Homeowners Ass'n v. Halfmann*, 535 S.E.2d 469, 474 (Va. 2000). Testimony that is equivocal or speculative on this point cannot be used to satisfy this burden. *See Cohn v. Knowledge Connections, Inc.*, 585 S.E.2d 578, 582 (Va. 2003) ("Before the issue of proximate cause may be properly submitted to the jury, . . . the evidence proving a

[2] Ms. Ali testified at her deposition that in fact, had she seen the physician warning about DEAEs actually in place at the time that she took Cymbalta, it would have sufficiently warned her of the risk such that she would have been dissuaded from using the drug. *See* Ali Dep. at 94:17-96:5, 97:1-4, Ullman Decl. Ex. 18. This further indicates the strength and clarity of the discontinuation warning and undermines Ms. Ali's claim that additional information was needed to accurately convey the seriousness of the DEAE risk.

causal connection must be 'sufficient to take the question out of the realm of mere conjecture, or speculation, and into the realm of legitimate inference.'" (quoting *Beale v. Jones*, 171 S.E.2d 851, 853 (Va. 1970))); *see also Colville v. Pharmacia & Upjohn Co.*, 565 F. Supp. 2d 1314, 1322 (N.D. Fla. 2008) (observing of proximate cause in failure to warn cases: "A mere possibility of such causation is not enough; and when the matter remains one of pure speculation or conjecture, or the probabilities are at best evenly balanced, it becomes the duty of the court to direct a verdict for the defendant.") (applying Florida law) (citations omitted).

Under the learned intermediary doctrine, as interpreted in Virginia, the key question for purposes of the proximate cause analysis is whether the doctor's decision to *prescribe* the drug at issue would have been altered by a stronger warning. *See, e.g.*, *Kling*, 1994 WL 477815, at *2-3 (affirming summary judgment for lack of proximate cause where "[Prescriber's] deposition testimony did not establish that stricter warnings would have made any difference in his decision *to prescribe the drug*" and where "prescribing physician . . . provided no evidence that more explicit warnings would have altered his treatment plan" (emphasis added)); *Talley v. Danek Medical, Inc.*, 7 F. Supp. 2d 725, 730 (E.D. Va. 1998) ("[A] plaintiff must not only show that a manufacturer's warning was inadequate, but that such inadequacy affected the prescribing physician's *use* of the product and thereby injured the plaintiff." (emphasis added)), *aff'd*, 179 F.3d 154 (4th Cir. 1999); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 06-CV-2798, 2009 WL 2487305, at *15 (E.D.N.Y. July 27, 2009) (interpreting Virginia law) ("The plaintiff provides no evidence that the inadequacy of Lilly's warning affected [the] prescribing decisions with respect to [plaintiff's] Zyprexa treatment. Failure to warn of Zyprexa's side effects did not proximately cause weight gain or diabetes . . . ."). Courts across the country have applied the

same standard, including in granting summary judgment in Lilly's favor regarding the Cymbalta warning. *See McDowell*, 58 F. Supp. 3d 391, 407-10; *Carnes*, 2013 WL 6622915.[3]

Lilly's counsel asked Dr. Ahmed whether the information Plaintiffs claim should have been included in the label (information from the Perahia article) would have changed her decision to prescribe Cymbalta for Ms. Ali. Dr. Ahmed responded that although she would have paid attention to that information and although she would have reviewed it with Ms. Ali as part of her discussion of the package insert, *see* Ahmed Dep. at 165:13-166:15, Ullman Decl. Ex. 19, she could not speculate as to whether it would have changed her prescribing decision. *Id.* at 166:16-167:8 ("It's all speculation because you're asking me hypothetical questions. I can't answer those things."); *id.* at 106:8-17 ("I can't really speculate without -- you know, you can't ask me to guesswork, so, yeah. You can't guesswork, I mean."). Plaintiff's counsel did not ask Dr. Ahmed any similar, ultimate questions; instead, he confined his questioning to asking whether Dr. Ahmed would have changed her discussion with Ms. Ali. *See id.* at 145:2-146:8. But whether a prescribing doctor might have changed her discussion with a patient in the face of a different warning is not the proper inquiry under Virginia proximate cause law. The sole relevant inquiry is whether a plaintiff can successfully demonstrate that her prescriber would have made a different prescribing decision.

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[3] *See also Wheat v. Pfizer, Inc.*, 31 F.3d 340, 343 (5th Cir. 1994) (Louisiana law) ("Plaintiffs must demonstrate that '. . . but for the inadequate warning, the treating physician would not have used or prescribed the product.'"); *Motus v. Pfizer, Inc.*, 358 F.3d 659, 661 (9th Cir. 2004) (California law) ("[A] product defect claim based on insufficient warnings cannot survive summary judgment if stronger warnings would not have altered the conduct of the prescribing physician."); *McDowell*, 58 F. Supp. 3d at 408 (New York law) ("Summary judgment is appropriate where a plaintiff fails to establish that a prescribing physician's decision to prescribe a particular medication would have changed had a different warning been given.") *Solomon v. Bristol-Myers Squibb Co.*, 916 F. Supp. 2d 556, 570 (D.N.J. 2013) (Texas law) (granting summary judgment where prescribing physicians "would have not changed their prescription for Plaintiff even understanding the additional risks or questions of efficacy Plaintiff has raised").

Given this record, Ms. Ali cannot carry her burden of proof on the issue of proximate cause. *See, e.g., Gaghan v. Hoffmann-La Roche*, No. L-3319-04, L-3361-04, L-1246-06, 2014 WL 3798338, at *16-17 (N.J. App. Div. Aug. 4, 2014) (finding that "equivocal" prescriber testimony was insufficient to prove proximate cause). Dr. Ahmed affirmed several times that her answer to the ultimate question -- whether she would have changed her prescribing habits -- could be no more than mere speculation. Indeed, in the face of that uncertainty, she refused to provide an answer other than "it depends." Such speculation does not satisfy the proximate cause requirement that Ms. Ali show via legitimate inference, at a minimum, that a different warning would have changed her physician's decision to prescribe her Cymbalta.

C. Aspects of the Negligence Claim Other than Failure to Warn Are Unsupported Both Legally and Factually.

Plaintiffs' first causes of action are titled "Negligence" and allege that Lilly was "negligent in the design, manufacture, testing, advertising, marketing, promoting, labeling, supply, and sale of Cymbalta." *See* Compl., *Ali*, ¶ 39. The allegations supporting these claims, however, each focus on Lilly's conveyance of instructions or warnings materials related to the risks of the product. *See, e.g., id.* ¶ 39(a) ("Failed to provide proper warnings"), (b) ("Failed to provide warnings"), (c) ("Failed to provide adequate training and instructions"), (j) ("Recklessly, falsely, and deceptively represented or knowingly omitted . . . material facts"). Stripped of their introductory rhetoric, these are entirely negligent failure to warn claims, and should be so interpreted by the Court. *See Ball*, 963 F. Supp. 2d at 505-06 ("A bare allegation of a 'defect' is no more than a legal conclusion. . . . In short, the plaintiff must plead supporting facts.").

To the extent that Plaintiffs have asserted other types of negligence, moreover, they run afoul of Virginia law. To succeed on a negligence claim under Virginia law, a plaintiff must prove that a product is unreasonably dangerous by demonstrating that it is "defective in assembly

or manufacture, unreasonably dangerous in design, or unaccompanied by adequate warnings concerning its hazardous properties." *Morgen Indus., Inc. v. Vaughan*, 471 S.E.2d 489, 492 (Va. 1996). Other types of negligence claims may not stand. *See, e.g.*, *Sykes v. Bayer Pharms. Corp.*, 548 F. Supp. 2d 208, 215 (E.D. Va. 2008) (rejecting failure to test claim as outside three specified categories). Allegations of "negligent testing" or "negligent promoting" do not invoke permissible claims in Virginia; summary judgment should thus be granted on Plaintiffs' first claims insofar as they allege negligence other than defective design, manufacture, or warning.[4]

II. PLAINTIFFS' NON-NEGLIGENCE CLAIMS FAIL AS A MATTER OF LAW.

In addition to their claims that Lilly negligently failed to adequately warn their doctors of the risks of discontinuation symptoms, Plaintiffs bring claims against Lilly of "failure to warn"; "constructive fraud"; "actual fraud"; and "breach of implied warranty." Lilly is entitled to summary judgment on each.

A. Failure to Warn

Plaintiffs' third cause of action in their complaints is denominated "Failure to Warn." To the extent that this cause of action overlaps with their negligent failure to warn claims, above, it is redundant. To the extent that this claim is intended to rely on a theory of strict liability, it must be dismissed: Virginia law "does not permit tort recovery on a strict-liability theory in products-

[4] One of the allegations Plaintiffs make in support of their "negligence" claims does appear to invoke defective design: "h. Negligently designed Cymbalta in a way that it knew would cause withdrawal and physical dependency." Compl. ¶ 39(h). Plaintiffs have previously conceded that they were "willing to withdraw their design defect counts." Pl.'s Resp. to Mot. for J. on the Pleadings at 9, *Ali*, Dkt. 75 (Apr. 21, 2015). The Court should accordingly disregard this allegation. Additionally, such claims are both preempted, *see Mutual Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013), and unsupported by any facts showing that Cymbalta fails to meet prevailing safety standards in its design, rendering it under Virginia law a reasonably safe product not subject to design defect claims. *See Talley*, 7 F. Supp. 2d at 731 ("[A] manufacturer is only required to design products that meet prevailing safety standards at the time the product is made.") (citing *Redman v. John D. Brush & Co.*, 111 F.3d 1174, 1177 (4th Cir. 1997)).

liability cases." *Sensenbrenner v. Rust, Orling & Neale, Architects, Inc.*, 374 S.E.2d 55, 57 n.4 (Va. 1988); *see also Harris v. T.I. Inc.*, 413 S.E.2d 605, 609-10 (Va. 1992); *Holmes v. Wing Enters., Inc.*, No. 1:08-cv-822, 2009 WL 1809985, at *7 n.14 (E.D. Va. June 23, 2009).

B. Breach of Implied Warranty

As with negligence, a plaintiff may recover under a breach of implied warranty theory only by showing "that the goods were unreasonably dangerous either for the use to which they would ordinarily be put or for some other reasonably foreseeable purpose." *Morgen Indus., Inc.*, 471 S.E.2d at 492; *see also Logan v. Montgomery Ward & Co.*, 219 S.E.2d 685, 687 (Va. 1975). And as with negligence, the only three ways in which the product may be unreasonably dangerous are a design defect, a manufacturing defect, or inadequate warnings. *See Morgen Indus., Inc.*, 471 S.E.2d at 492. As demonstrated above, Lilly is entitled to summary judgment on Plaintiffs' allegations both of inadequate warnings and defective design. *See* Section I.A-B, *supra*. (There is no manufacturing defect claim being asserted.) Accordingly, summary judgment should be granted on their implied warranty claim as well.

C. Constructive Fraud

Plaintiffs' claims for constructive fraud fail because they can establish neither falsity nor reliance. A finding of constructive fraud must rest on "clear and convincing evidence that one has represented as true what is really false, in such a way as to induce a reasonable person to believe it, with the intent that the person will act upon this representation." *Mortarino v. Consultant Eng'g Servs., Inc.*, 467 S.E.2d 778, 782 (Va. 1996) (quoting *Evaluation Research Corp. v. Alequin*, 439 S.E.2d 387, 390 (Va. 1994)).

Plaintiffs claim that "Lilly represented . . . that Cymbalta was safe for use and that any withdrawal symptoms were no different, no worse, and no more frequent, than those of other similar products on the market." Compl., *Ali*, ¶ 71. This general, conclusory allegation is

unsupported by fact. First, Lilly makes no generic representation in its labeling that Cymbalta is "safe for use." Instead, the labeling provides "the information needed to use Cymbalta safely and effectively" -- including information about the risk of discontinuation symptoms. *See* 2011 Label at 1. FDA's approval hinges on whether a drug has been demonstrated to be "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof," a test that Cymbalta passed in its repeated approvals from the agency. 21 U.S.C. §§ 355(c)(A), 355(d). As courts around the country have recognized, moreover, there is a "well-established principle that 'safe and effective' are relative terms in the pharmaceutical industry -- 'safe' drugs harm some people and 'effective' drugs do not work in every case. *In re Avandia Pracs. & Prods. Liab. Litig.*, 588 F. App'x 171, 177 (3d Cir. 2014). Lilly's actual warning, as set forth in its label, was specific and detailed in identifying the general risk of discontinuation symptoms and stating the frequency of particular symptoms. *See* 2011 Label § 5.7, Ullman Decl. Ex. 1.

Second, the label makes no relative comparisons about the frequency or severity of discontinuation symptoms between Cymbalta and other drugs, as Ms. Ali alleges. In fact, the label identifies a particular set of symptoms as having occurred with a given frequency in Cymbalta clinical trials and an overlapping, but non-identical set of symptoms as having been reported for other drugs -- a representation which is neither false nor indicative of the symptoms being "no different" than those of other drugs. *See id.*; Compl., *Ali*, ¶ 71.

Moreover, Ms. Ali has not sufficiently demonstrated that either she or her physician relied on alleged misrepresentation regarding Cymbalta. Ms. Ali admitted that, based on Lilly's warnings, she would not have taken Cymbalta. *See* Ali Dep. at 94:17-96:5, 97:1-4, Ullman Decl. Ex. 18. She cannot, therefore, support a claim that Lilly's warning language *induced* her to take Cymbalta. Similarly, Dr. Ahmed testified that she did not know what she would have done

differently had she been provided with statistics from the Perahia article, figures that Ms. Ali alleges are misleadingly missing from Lilly's warning. Compl. ¶ 71; Ahmed Dep. at 105:17-107:5, Ullman Decl. Ex. 19. This does not create a genuine issue of material fact as to whether Dr. Ahmed relied on Lilly's supposed misrepresentation in prescribing Cymbalta to Ms. Ali.

Likewise, Ms. Hagan-Brown, who testified that she still *would* have taken Cymbalta even given Plaintiffs' desired warning, cannot be found to have relied on Lilly's alleged misrepresentation in deciding to take the drug. *See* Hagan-Brown Dep. at 200:13-204:12, Ullman Decl. Ex. 24.

D. Actual Fraud

In order to prevail on an actual fraud claim, Plaintiffs must prove "by clear and convincing evidence '(1) a false representation, (2) of a material fact, (3) made intentionally and knowingly, (4) with intent to mislead, (5) reliance by the party misled, and (6) resulting damage to the party misled.'" *Hitachi Cred Am. Corp. v. Signet Bank*, 166 F.3d 614, 628 (4th Cir. 1999) (quoting *Alequin*, 439 S.E.2d at 390). Although omission of a material fact may give rise to a claim of actual fraud, that omission must rise to the level of concealment -- that is, "deliberate nondisclosure designed to prevent another from learning the truth." *See id.* at 629. "Fraud by concealment requires actual intent to conceal a fact." *Carlucci v. Han*, 907 F. Supp. 2d 709, 740 (E.D. Va. 2012). In ruling on a motion for summary judgment, the Court must take into account the "clear and convincing" standard of proof for fraud claims. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 254-55 (1986).

Although Plaintiffs allege specific acts in support of their actual fraud claims, they have failed to demonstrate reliance on any acts outside the label, and there is no evidence Lilly made any allegedly false statement with knowledge of its falsity or intent to mislead.

1. Plaintiffs demonstrate no reliance on any Lilly documents or statements outside the label.

Of the acts alleged by Plaintiffs, *see* Compl. ¶ 82, the majority constitute assertions related to Cymbalta's marketing, published clinical trials, and medical journal articles by individuals who were at one time Lilly consultants. There is no evidence in the record to suggest that Plaintiffs' prescribing physicians were influenced by any of the alleged false statements Plaintiffs identify: Lilly advertising or marketing materials about Cymbalta (Compl. ¶ 82(b), (c), (e); the Practice Guideline for the Treatment of Patients with Major Depressive Disorder (3d ed.) (Compl. ¶ 82(c)); a 2006 article by Alan F. Schatzberg in the Journal of Clinical Psychiatry (Compl. ¶ 82(g)); the American Psychiatric Publishing Textbook of Psychiatry (5th ed. 2008) (Compl. ¶ 82(h)); or scientific literature about Cymbalta published by Lilly (Compl. ¶ 82(i)). Similarly, Plaintiffs have not alleged with the requisite specificity that they encountered any particular misrepresentation in Lilly's marketing or advertising materials and that such misrepresentations caused them to take Cymbalta, or that they came into contact with the broader scientific and medical literature that allegedly contains misrepresentations. Any statements supporting Plaintiffs' claims of fraud, therefore, must be limited to those in the label -- the only document with which Plaintiffs can establish they and their prescribing physicians came into contact. And, as discussed above, the testimony of Ms. Ali, Dr. Ahmed, and Ms. Hagan-Brown all establishes that they did not rely on the discontinuation warnings in Lilly's label either.

2. There is no evidence that Lilly made any allegedly false statement with knowledge of its falsity or an intent to mislead.

If the Court finds that Lilly is entitled to summary judgment on Plaintiffs' negligent failure-to-warn claims, Lilly is equally entitled to summary judgment on their fraud claims. But even setting aside the accuracy of the label's representations, Plaintiffs have no evidence that Lilly knew they were false or intended to mislead, or that they reflected concealment. In fact,

Plaintiffs' regulatory expert, Dr. Louis Morris, admitted that he did "not have any -- any sense that [Lilly was] trying to hide information. . . . I don't think that this was information that they were trying to hide." Morris Dep. at 183:16-184:17, Ullman Decl. Ex. 30.

Dr. Morris's opinion that Lilly did not intend to conceal or mislead reflects the disclosure that Lilly undertook with respect to the information it had available about discontinuation symptoms. It is undisputed that Lilly affirmatively disclosed the results of its Cymbalta clinical testing, including the data it had collected on DEAEs, to the FDA to obtain approval, and that it continued to do so after the approval of the medication. *See* Complete Response to FDA Approvable Letter NDA 21-427, App. 9.2.9, Ullman Decl. Ex. 8; Reports of Analyses of Data from More than One Study for Cymbalta (Duloxetine hydrochloride) Chronic Pain tbls. 3.36 & 3.37, Ullman Decl. Ex. 9. These results included the specific statistics that Plaintiffs allege were fraudulently withheld from the Cymbalta label. *See* CYM-00708137. This kind of data exchange with FDA "belies any inference of fraud" as it pertains to the label. *See Torkie-Tork v. Wyeth*, 739 F. Supp. 2d 908, 910-11 (E.D. Va. 2010).

Lilly not only shared its data with the FDA, it published the results of these studies for review by other scientists and medical providers. *See* Allgulander et al., *supra*, Ullman Decl. Ex. 10; Perahia et al., *supra*, Ullman Decl. Ex. 11. Plaintiffs' claims that Lilly fraudulently concealed information about the rates and severity of discontinuation symptoms hinge on information they obtained from the publicly-available Perahia article. Even Plaintiffs' claim that Lilly's studies were improperly or fraudulently designed because they did not use a "withdrawal symptom checklist," *see* Compl. ¶ 82(d), is based on the disclosure in the Perahia article that lack of a checklist was the "main limitation" of the review. *See* Perahia et al., *supra*, at 211.

Claims of fraud premised on concealment cannot survive when the information allegedly concealed was publicly disclosed and disseminated to both the regulating agency and to the community of scientists and medical providers at large. There is no evidence that Lilly's choice of language in its discontinuation warning was premised on anything other than compliance with FDA's guidelines about labeling. As a result, Lilly is entitled to summary judgment on Plaintiffs' fraud claims.

CONCLUSION

Plaintiffs Janine Ali and Gilda Hagan-Brown cannot demonstrate that there are genuine disputes of material fact that prevent Lilly from being entitled to judgment as a matter of law on their claims. For the reasons set forth above, Lilly respectfully requests that the Court enter summary judgment in its favor.

Dated June 29, 2015

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on the 29th day of June, 2015, I will electronically file the foregoing with the Clerk of the Court using the CM/ECF system, which will then send a notification of such filing (NEF) to the following:

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